Remarks

Claims 68-74, 76-119, 122-127, 129 and 132-140 are pending in the above-identified patent application. Applicants respectfully request reconsideration in view of the remarks below.

35 U.S.C. § 103 –Weiner and Rosenman

The Office rejected claims 68-74, 76-91, 93-97, 99-109, 111-119, 122-127, 129 and 132-140 under 35 U.S.C. 103(a) as assertedly being unpatentable over Weiner *et al.*(U.S. Patent No. 5,466,233; herein "Weiner") in view of Rosenman *et al.* (U.S. Patent No. 6,478,776; herein " Rosenman").

Applicants continue to traverse the rejection. The Office action and cited art do not support a *prima facie* case of obviousness against the current claims and the rejection under 35 USC 103 should be withdrawn.

Weiner does not teach a non-linear shaped body member

The Office characterizes Weiner as disclosing, "an implantable ocular drug delivery device (10) having a non-linear shaped body member (12, 14a) comprising a tube and that is implanted within a patient eye to deliver a drug substance to the patient via the body member and a cap element (16) (see Figures 1-5)." Applicants' response of 12/16/10 stated that the non-parallel surfaces 70 of Weiner's cone-shaped cap (figure 1) and rounded ends 26 of the test tube-shaped embodiments (figures 2-5) *do not* amount to non-linear shaped body member as claimed. Applicants maintain this position. As understood by the current application, a non-linear body member deviates from a linear path (see, for example, page 7, lines 21-26), such as a coil shape. To understand if a body member is linear or non-linear one must follow the "longitudinal axis" of the device (col. 5, line 35 of Weiner refers to longitudinal axis), not a device surface. The longitudinal axes of Weiner's tack embodiments are linear, not non-linear.

To this the Office has argued that, "The broadest reasonable interpretation has been applied to a "nonlinear shaped body member to indicate a body member which has a surface which does not follow a straight line. Applicant's arguments, that to understand if

a body member is linear or non-linear, the "longitudinal axis" of the device must be followed, are not persuasive as the surface of the device can also be followed to determine if a body member has a linear shape or a non-linear shape."

According to MPEP 2111, during patent examination, while the pending claims must be given their broadest reasonable interpretation, *the interpretation must be consistent with the specification.* The interpretations that Weiner's conical or post-shaped implant corresponds to a body member having a non linear shape as claimed is not consistent with Applicants' specification. For example, the Office has not pointed to any particular portions of the Applicants' specification otherwise supporting an argument that a conical or post-shape (as described by Weiner) corresponds to a non-linear body member as claimed.

Rather, Applicants' specification has distinguished the linear shaped body members as described by Weiner in Applicants' background section on page 3, lines 15-20:

> *U.S. Pat. No. 5,466,233 describes a certain tack for intraocular drug delivery. This device has an end that is positioned in the vitreous cavity while the head remains external to the eye and abuts the scleral surface. The tack contains a fixation portion to attempt to retain attachment within the eye. Because the overall shape of the capsule is linear, the amount of drug that may held by the device and the surface area through which the drug may be delivered is limited. (underlining our emphasis)*

A non-linear shaped body member according to the Applicants claims is not taught or suggested by Weiner.

Modification of Weiner's conical or plug-shaped implant to a non-linear coil shape would take away an advantage of Weiner's insertion process

Applicants maintain that Weiner does not provide sufficient motivation to modify the shape of its body member from linear to non-linear. Rather, Weiner teaches that a linear body member allows for a substantially straight insertion and this is preferred. As stated by Weiner:

> *In the preferred method of insertion, the tack 10 of the present invention is inserted into the eye 18 by injection. While the tack 10 may be inserted by hand*

> *into the sclera 24, injection is preferred as it helps to prevent risk of accidental damage or abrasion to the scleral surface 28. In addition, injection provides for a substantially straight insertion. As shown in FIG. 15, the tack 10 may be injected by loading the tack 10, with the first end 22, 26 of the post 12 pointed toward a first end 84 of the syringe 82 and the head 16 abutting the plunger 86 of the syringe 82 when the plunger is in a fully extended position. (underlining our emphasis)*

The process using the arrangement of Figure 15 of Weiner is described in greater detail in column 15, lines 20-45. In this process the tack is essentially inserted straight through the scleral tissue so the post passes right into the vitreous. The Office has responded by stating that "Weiner et al also disclose that it is preferred that the device (10), which has a non-linear shaped body member (12, 14a) is inserted with a "slight twirling motion" (lines 2-4 of column 15)." In response to this, a "slight twirling motion" still would not suggest a non-linear device because even if it was done, such motion would only result in movement of the Weiner's cone or plug-shaped implant around its linear longitudinal axis (col. 5, line 35). Therefore, this does not change the fact that the *linear configuration* of Weiner's device provides for a substantially straight insertion. The straight insertion method described in column 15 and shown in Figure 15 of Weiner results in the implant going directly through the scleral tissue (i.e., the linear longitudinal axis is perpendicular to the scleral tissue at the point of implant entry). On the other hand, the non-linear configuration of the Applicants' claimed device results in the body member passing through the scleral tissue at an angle. Applicants' insertion is fundamentally different from Weiner's because Applicants use a non-linear shaped body member and Weiner does not.

The advantageous substantially straight insertion method, for example, using the arrangement of Figure 15 of Weiner, could not be achieved by modifying the Weiner's device to a non-linear shape. Replacing Weiner's cone or post with a coil-shaped device, such as Rosenman's, as the Office is suggesting, would cause scleral tissue damage. A coil being pushed straight through the scleral tissue, without the proper form of insertion that is described only in the Applicants' specification, would result in tissue damage.

Modification of Weiner's plug-shaped implant to less than 1 mm and to make it less than this would limit the amount of drug that could be loaded and this goes against wieners teaching

Weiner makes no suggestion to modify its device to provide a cross sectional diameter of the body member of 0.5 mm or less, or a diameter in the range of 0.25 mm to 0.5 mm, according to Applicants claims 139 and 140, respectively. Rather, Weiner suggests a diameter between 1 mm and 4 mm. To this, the Office has replied: "As seen in Figures 1 and 5, both the conical and the capsule shaped tube or post (12) have a cross-section at the first end (22 or 26) of the tube or post (12) that is less than the diameter at the second end. Therefore, the tube or post (12) of Weiner et al has a cross-section of 0.5 mm or less in diameter or has a circular cross-section in the range of 0.25 to 0.5 mm in diameter at the first end (22 or 26) of the tube or post (12) as, when the cross-section of the second end (40) is about 1 mm in diameter, the cross- section at the first end (22 or 26) will be 0.5 mm or less in diameter as seen in Figures 1 and 5."

In response to this Applicants note that what is currently being claimed is a "tube", not a cone shaped device. The post-shaped device of Weiner is not taught as having a cross sectional diameter of less than 1 mm. The Office's argument that Weiner teaches a cross sectional diameter of the body member of 0.5 mm or less merely because the distal end of the device is "rounded," is implausible and not supported by the teaching of any of the cited references, nor the Applicants' own specification.

To reduce the cross-sectional diameter would considerably limit the amount of drug that could be placed in Weiner's device, and this would be contrary to the teaching of Weiner, which is to provide sustained drug delivery device that is capable of staying positioned in the vitreous region (see column 1, lines 19-26; column 2, lines 40-50; and column 6, lines 33-41).

Rosenman does not teach that its head structure is insertable through an incision approximately the same size as the outer diameter of the tube forming the body member.

The Office action repeats throughout..."Since the device of Rosenman et al is insertable through an incision approximately the same size as the outer diameter of the tube forming the body member...," but this is not correct. An incision is made using some sort of blade or scalpel

to cut tissue (see, for example, Weiner column 14, line 62, to column 15, line 3). Applicants point out that nowhere in Rosenman is found the term "incision." Rather, in column 11, lines 39-43, Rosenman teaches that the surgeon inserts the delivery catheter into the patient's vasculature through the skin, typically entering the femoral artery. The process of making an "incision" cannot be performed at the cardiac tissue site. Therefore, if any incision is made in Rosenman it must be at the femoral artery entry site and large enough to accommodate the entire width of the catheter, which is substantially larger than the width of the body member of the cardiac implant. (See Figures 18 and 19 of Rosenman.)

Rosenman does not teach or suggest using its implants for ocular drug delivery

There is nothing in Rosenman that teaches using its myocardial implants for delivery of drugs to the eye. While the Office action states: "Rosenman et al disclose implanting the device within the heart and other organs of the body which can include the eye (lines 8-28 of column 16)," what is only taught in Rosenman at lines 8-28 of column 16 is exactly the following:

> *While the devices and methods have been described in relation to the treatment of the heart and treatments for ischemia with implantation of a helix or dart loaded with an angiogenic agent, they may be adapted to treat other conditions within the heart, other organs of the body, and conditions such as tumor and cancers. For example, the coils or darts or implants of other shapes can be adapted for implant into a tumor and loaded with a tumor necrosis factor. Many compounds may be loaded into the implants. "Angiogenic agents" and "endothelial agents" including the following may be used: insulin like growth factor-I (IGF-I), VEGF, VIGF, PDGF, epidermal growth factor (EGF), CTGF and members of its family, FGF, TGF-a and TGF B; the widely recognized angiogenic agents VEGF-165, VEGF 121, VEGF-145, FGF-1, FGF-2, Transforming Growth Factor (TGF-B), Tumor Necrosis Factor a (TNF-a), Tumor Necrosis Factor B (TNF-B), Angiogenin, Interleukin-8, Proliferin, Prostaglandins (PGE), Placental Growth factor, Granulocyte Growth Factor, Platelet Derived Endothelial Cell Growth Factor, Hepatocyte Growth Factor, DEL-1, Angiostatin-1 and Pleiotrophin.*

There is no term "eye", "ocular," "ophthalmic", or any term specifically describing eye anatomy in this passage.

One of skill in the art of intraocular drug delivery would not have been familiar with the teaching of Rosenman at the time of the invention because Rosenman is directed to cardiac drug delivery

Applicant continues to point out that the eye is an anatomically unique area of the

body, which presents particular considerations for the delivery and treatment with a bioactive agent. Given these unique properties, one of skill in the art of ocular drug delivery would not have looked towards devices designed for use in cardiac tissue as taught by Rosenman. Applicants have argued that one of skill in the art of ocular drug delivery would be, for example, an ophthalmologist. An ophthalmologist does not practice cardio thoracic surgery, nor would have been expected to have been familiar with particular cardiovascular technologies, such as described by Rosenman. To this the Office has replied that, "...an ophthalmologist or a surgeon using the device of Weiner et al would be familiar with the general field of implantable devices for delivering drugs into a patient's body, and, thus, would be familiar with the implantable devices such as those taught by Rosenman et al."

Applicants disagree. The Office appears to be stating that an ophthalmologist would have knowledge of all documents describing implantable medical devices for drug delivery, including those specifically used for delivering drugs to an the eye, as well as the vast number of those documents such as Rosenman that do not discuss ocular drug delivery. Respectfully, Applicants find no support for this assertion. Applicants also disagree with the implication that Rosenman is directed to "the general field of implantable devices for delivering drugs;" rather, Rosenman is primarily focused on myocardial implants and the treatment heart diseases using these myocardial implants, which is discussed further herein.

Many of the complexities of ocular drug delivery are described in Applicants' background section, for example, see page 1, lines 18-30. Given the unique properties of the eye, one of skill in the art of ocular drug delivery would not have looked towards devices designed for other areas of the body in attempts to address unique challenges associated with ocular drug delivery.

Rosenman is in a dissimilar area of medical treatment as it is directed to the treatment of heart tissue. Because of the fundamentally different anatomic concerns between the eye and the heart, Weiner and Rosenman cannot be considered to be in the same field of endeavor.

Rosenman's teaching is overwhelmingly directed to myocardial implants and the treatment heart diseases using these myocardial implants. With regards to "other organs of the body" used at column 16, line 12, the only other tissues that are specifically called out by Rosenman are at column 16, line 13, which are tumor and cancers. While Rosenman actually uses the term "cardiac" and cardiac-terms recurrently, the term "other organs of the body" is used very infrequently; however, the Office action represents the teaching of Rosenman just the opposite. Applicants do not see this as a proper characterization of the teaching of Rosenman by the Office.

The Office also fails to explain with any convincing reasoning why it believes the anatomy of myocardial tissue or that of a tumor so similar to the anatomy of an eye that, at the time of the invention, one would consider using Rosenman's myocardial implant in place of Weiner's ocular tack. As discussed in the Applicants' previous responses, Rosenman's implant is entirely surrounded/buried within the solid tissues of the heart, and therefore any portion of its implant can provide stabilization in the surrounding solid tissue. But, as the Applicants have pointed out, there are fundamental anatomical differences between the heart and eye, and one of skill at the time of the invention would have no clear motivation to make such a substitution.

The claims are non-obvious because the problem solved by the Rosenman technology does not correlate to the problem solved of the current invention

A problem solved according to the current invention is substantially increasing the drug load for intraocular drug delivery, while not obscuring the central visual field, while concurrently minimizing disruption to ocular tissue during the implantation process. On the other hand, as conveyed in column 3, lines 35-67, Rosenman addresses particular problems in the area of cardiac drug delivery for the treatment of heart disease. Rosenman states that prior art polymeric microsphere formulations used for the treatment of heart disease were problematic because they do not provide optimal release kinetics, they can escape into the arterial blood system, and they can also increase the risk of embolic events. Therefore, the problem solved according to Rosenman is providing an implant that contains the drug substance during its delivery to the myocardium and residence there so that problems of drug not being at the correct location for cardiac

treatment in the body are avoided. Importantly, the Rosenman myocardial implant is not required to have a non-linear or coiled shape. For example, the cardiac implants shown in Figures 24, 25, and 26 of Rosenman have a linear configuration (dart-like), and do not have a non-linear or coiled shape. Yet these linear dart-shaped implants of Rosenman still solve the problems of cardiac drug delivery. Therefore, the non-linear coil-like configuration is not critical to solving the cardiac drug delivery problem discussed in Rosenman. In reference to *In re Oetiker*, 977 F.2d 1443 24 USPQ2d 1443 (Fed. Cir. 1992), if the prior art reference is not in the Applicants' field of endeavor, it must be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention.

This is another indication of non-obviousness – the problem that Rosenman solves with its technology is not reasonably pertinent to the particular problem with which the Applicants were concerned. Without the guidance of the Applicant's own specification, there would have been no reason to identify the coil shaped design of Rosenman's myocardial implant and use it instead of the plug-shaped body member.

35 U.S.C. § 103 – Weiner, Rosenman, and Johnson

The Office rejected claims 92, 98 and 110 under 35 U.S.C. 103(a) as assertedly being unpatentable over Wiener *et al.* in view of Rosenman *et al.* as applied to claims 83, 93 and 99 above, and further in view of Johnson (U.S. Patent No. 5,972,027; herein "Johnson").

Applicants continue to traverse the rejection. As discussed above, Weiner and Rosenman fail to teach or suggest Applicants' claimed devices or methods. Johnson is cited for allegedly describing shape memory materials. However, Johnson does not remedy the above-noted deficiencies in Weiner and Rosenman. Accordingly, the pending claims are patentable over Weiner and Rosenman and Johnson.

Conclusion

It is respectfully submitted that this communication is fully responsive to the current final Office Action. The Examiner is invited to telephone the undersigned in the event that such communication is deemed to expedite prosecution of this application.

Respectfully Submitted,

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